II. The Present Amendment

No new matter is added by the present amendment.

The amendments to claim 7 rewrite the claim as an independent claim by incorporating a recitation from the claim from which claim 7 formerly depended and clarify the order of the steps. The amendments to claims 8 and 16 conform their antecedence to preceding claims. The amendment to claim 15 rewrites the claim in independent form.

New claim 35 recites the steps of claim 7, with a recitation similar to that requested by the Examiner with regard to claim 7. New claims 36 to 42 track original claims 8-14. New claim 43 recites claim 15 as amended, with a recitation similar to that requested by the Examiner with regard to claim 15. New claims 44 to 45 track original claims 16-17.

III. The Office Action

The Action rejects the claims on several grounds. For the Examiner's convenience, the rejections are discussed below in the order in which they are presented in the Action.

A. Rejections under 35 U.S.C. § 112, second paragraph

Claims 7-18 are rejected under 35 U.S.C. § 112, second paragraph as indefinite.

1. Claims 7 and 15 are stated to be indefinite because they depend from cancelled claim 1. This rejection has been obviated by introducing into the claims the relevant recitations from claim 1.

2. Claims 8 and 16 are rejected for improper antecedence. The rejection has been obviated by amending the antecedence.

Applicants note for the record that the above amendments are not made to overcome any rejection over the art and that no equivalents are intended to be surrendered thereby.

B. Rejections under 35 U.S.C. § 102(b)

Claims 7-10 and 13-18 are rejected under 35 U.S.C. § 102(b) as anticipated by Baxter-Lowe, U.S. Patent No. 5,486,611 ("Baxter-Lowe"). According to the Action, column 3, lines 35 on of Baxter-Lowe disclose HLA typing which includes amplifying an HLA sequence of DNA and detecting the formation of a DNA duplex between the labeled probe and HLA sample sequence. Action, at page 3. The Action further indicates that Table 2, residues "63+" shows a peptide reading on the claimed invention. *Id.* Applicants traverse.

As the Examiner is aware, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051 (Fed. Cir. 1987) and MPEP §2131. The Action attempts to recreate claim 7 by stitching together certain aspects of Baxter-Lowe to find each and every element of the claim present in the reference. The language of Baxter-Lowe, however, does not permit the reading suggested by the Action.

Claim 7 recites as element (a) "contacting the sample with an oligonucleotide primer pair capable of amplifying a subsequence of an MHC nucleic acid" and, as element (b), amplifying the nucleic acid. The method steps therefore recite a temporal sequence in which the sample is first contacted with a primer pair and then amplified. To emphasize this, a phrase has been added reciting that the steps are performed in the order shown.

In contrast, Baxter-Lowe, at the place cited by the Action (column 3, lines 35 on) indicates that the method for HLA typing includes, in relevant part, the steps of: "(a) amplifying an HLA sequence of DNA of a human subject; (b) bringing a labelled oligonucleotide probe . . .into contact with a sample of the amplified HLA sequence . . . [and] (c) detecting the formation of a DNA duplex between the labelled probe and the HLA sample sequence . . . . " In short, the passage of Baxter-Lowe cited by the Action discloses a method in which an HLA sequence is amplified, the amplified sequence is

then contacted with a labelled probe, and the formation of a DNA duplex is then detected. The order of the steps is different, and it is therefore not the same method. Thus, Baxter-Lowe does not teach all the elements of the invention as claimed, and is not a proper reference for purposes of § 102(b).

Similarly, Baxter-Lowe does not anticipate claims 15-18. As already noted, to be a proper reference for purposes of §102(b), the reference must contain every element of the claim. The Action alleges that Table 2 anticipates the claim because residues 63+ allegedly sets forth a peptide reading on the invention. But the Action fails to show that Baxter-Lowe sets forth primer pairs capable of amplifying a subsequence of an MHC nucleic acid which subsequence encodes a polypeptide comprising a peptide of SEQ ID NO:2. Accordingly, the Action has failed to show a prima facie case of anticipation.

Although Baxter-Lowe has not also been cited as rendering the invention obvious under § 103(a), for extra measure, Applicants note that Baxter-Lowe does not render the present invention obvious. Baxter-Lowe amplifies HLA before contacting them with a labeled probe to provide sufficient amounts of the amplified HLA sequence to conduct sequence-specific oligonucleotide probe hybridization ("SSOPH"). It is the use of SSOPH following amplification that permits the detection of polymorphic residues (see, Baxter-Lowe at column 4, lines 2-12) and that, coupled with the use of control sequences to detect false positives and negatives provides the novelty of the Baxter-Lowe method over the prior art (see, column 3, lines 23-34). It is impermissible to modify a reference in a manner that would destroy its purpose, as would be necessary to modify the Baxter-Lowe method to recreate the present invention. Accordingly, Baxter-Lowe neither teaches nor suggests the method as claimed herein.

Applicants have also introduced new claims 35-42 herein. Claim 35 tracks claim 7 as amended, but includes an additional recitation that the MHC nucleic acid subsequence encodes a polypeptide consisting essentially of a peptide having a structure recited by the claim. The Action does not contend that Baxter-Lowe teaches the use of primer pairs that amplify a subsequence of an MHC nucleic acid consisting

essentially of the sequence recited in the claim. Indeed, even under the Action's too-expansive reading of Baxter-Lowe, the Action concedes that claim 7 amended to recite "consisting of" the claimed sequence would overcome the rejection. The Examiner will appreciate that the "consisting essentially of" language likewise avoids Baxter-Lowe. Accordingly, Applicants submit new claim 35 is patentable over Baxter-Lowe, and that new claims 36-42, which depend from claim 35, are likewise patentable.

C. Rejections under 35 U.S.C. § 103(a)

Claims 15-18 are rejected under 35 U.S.C. § 103(a) over Mottez, U.S. Patent No. 5,976,551 (hereafter, "Mottez"). According to the Action, Mottez discloses SEQ ID No. 115, which reads on the peptide of the instant invention. See amino acid residues 70+ for an exact match to the sequence of claim 15." Action, at page 4. Applicants traverse the rejection.

Applicants respectfully submits that the Action fails to set forth a proper *prima facie* case of obviousness. Mottez SEQ ID NO:115 is a 266 amino acid sequence (see, sequence listing at column 163 of Mottez), which the specification indicates is the sequence of a particular representative class II β chain deduced from a cDNA clone. *See*, Mottez specification at columns 43-44 and Table at columns 45-46. In contrast, the kits of claim 15 comprise "an oligonucleotide primer pair capable of amplifying a subsequence of an MHC gene or gene product." Thus, the claim does not recite a peptide, as asserted by the Action. Mottez is concerned with compositions of polypeptides "with altered MHC class II determinants" comprising various domains to form a complex recognizable by a T cell receptor. Mottez does not appear to teach primer pairs to amplify nucleic acids encoding any peptide at all. It certainly does not teach primers to amplify even the 266 amino acid sequence of SEQ ID NO:115, let alone the "**subsequence** of an MHC gene or gene product" as recited by the claims under examination.

Moreover, even assuming that the 266-amino acid sequence of SEQ ID NO:115 constitutes a "MHC gene product," the Action fails to show that there is any

motivation for one of skill to create primers to a nucleic acid encoding a subsequence of that sequence. As defined in the specification at page 11, lines 29-31, the term "subsequence of a Class II major histocompatibility molecule" refers to a polypeptide or peptide that has a sequence that is ***less than*** a naturally occurring full length sequence of a Class II MHC polypeptide. The language of the claim therefore does not encompass a kit that contains primers amplifying only the full length 266-residue sequence of SEQ ID NO:115. Yet, the Action fails to show any motivation to create primers to a subsequence of that sequence. The Action does not even allege, let alone show, that motivation to create the claimed primers exists, as would be required to set forth a proper *prima facie* case under § 103(a).

Applicants respectfully remind the Examiner that the burden rests upon the Examiner to present a proper *prima facie* of obviousness. Applicants respectfully submit that the Action has failed to meet this burden with respect to kits comprising "an oligonucleotide primer pair capable of amplifying a subsequence of an MHC gene or gene product," as recited in claim 15.

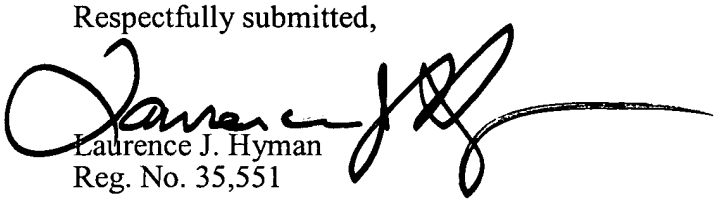
Finally, the Action rejects claim 18 on the ground that it recites instructional material. According to the Action, printed matter on a label or package insert cannot confer patentable weight as a limitation on a product. Action, at page 5. The Action supports this contention with citations to *In re Haller*, 73 USPQ 403 (CCPA 1947), which the Action characterizes as holding that printed matter to a new use cannot render old matter patentable. Applicants respectfully observe that, since the Action has failed to set out a prima facie case of obviousness as to the kit of claim 15, the Examiner has failed to meet the Examiner's burden to show that Applicant is not entitle to a patent. Claim 18 therefore merely adds an additional recitation to an already patentable invention. The Action does not allege that *Haller* says that printed matter cannot properly add an additional recitation to a composition or article which is itself new and patentable, as with the kits of the present invention.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

7. (Amended) A method for detecting a nucleic acid in a biological sample, wherein the nucleic acid encodes a peptide capable of specifically binding to a Lym-1 antibody, the method comprising the following steps, in the following order:

(a) contacting the sample with an oligonucleotide primer pair capable of amplifying a subsequence of an MHC nucleic acid, which subsequence encodes a polypeptide comprising a peptide [of claim 1,] having a sequence comprising R_1 - R_2 - R_3 - R_4 - R_5 - R_6 - R_7 - R_8 - R_9 - R_{10} - R_{11} - R_{12} - R_{13} - R_{14} - R_{15} - R_{16}, wherein R_1 is Gln, Lys, or Arg; R_2 is Arg; R_3 and R_4 are members independently selected from the group consisting of all amino acids; R_5 is Ala, Glu, Asp, Val, Leu or Ile; R_6 and R_7 are members independently selected from the group consisting of all amino acids; R_8 is Thr; R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{14}, and R_{15} are members independently selected from the group consisting of all amino acids; and, R_{16} is Val (SEQ ID NO:2);

(b) amplifying the nucleic acid; and

(c) detecting the amplified nucleic acid.

8. (Amended) The method of claim 7, wherein the MHC [gene] nucleic acid is HLA-DR 10.

15. (Amended) A kit for detecting a nucleic acid in a biological sample, wherein the nucleic acid encodes a peptide capable of specifically binding to a Lym-1 antibody, comprising an oligonucleotide primer pair capable of amplifying a subsequence of an MHC gene or gene product, which subsequence encodes a polypeptide comprising a peptide [of claim 1] having a sequence comprising R_1 - R_2 - R_3 - R_4 - R_5 - R_6 - R_7 - R_8 - R_9 - R_{10} - R_{11} - R_{12} - R_{13} - R_{14} - R_{15} - R_{16}, wherein R_1 is Gln, Lys, or Arg; R_2 is Arg; R_3 and R_4 are members independently selected from the group consisting of all amino acids; R_5 is Ala, Glu, Asp, Val, Leu or Ile; R_6 and R_7 are members independently selected from

the group consisting of all amino acids; R_8 is Thr; R_9, R_{10}, R_{11}, R_{12}, R_{13}, R_{14}, and R_{15} are members independently selected from the group consisting of all amino acids; and, R_{16} is Val (SEQ ID NO:2).

16. (Amended) The kit of claim 15, wherein the MHC [gene] nucleic acid is HLA-DR 10.